UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MEMORANDUM

DATE: June 23, 2011

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

SUBJECT: Science Review In Support of the Registration of Bug Oil Ornamental containing Canola Oil, Tagetes Oil, Thyme Oil and Wintergreen Oil as its active ingredients.

Decision Number:	420842
DP Number:	385633
EPA File Symbol Number:	85937-R
Chemical Class:	Biochemical
PC Code:	011332, 176602, 597800, 176601, respectively
CAS Number:	120962-03-0, 8016-84-0, 8007-46-3, 68917-75-9, respectively
Tolerance Exemptions:	40 CFR 180.950 for all active ingredients
MRID Numbers:	48329202-48329205, 48329207-48329209, 48339001-48339002

FROM: Angela L. Gonzales, Biologist 6/23/11
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

TO: Colin Walsh, Regulatory Action Leader
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

ACTION REQUESTED

In response to the request for additional information discussed in the memorandum from A.L. Gonzales to C. Walsh dated 8/25/10 and relayed in a letter to the registrant dated 9/9/2010, the registrant has submitted a revised Confidential Statement of Formula (CSF) dated December 20, 2009, product chemistry information in MRIDs 48329207, 48329208 and 48339001, mammalian toxicology information in MRIDs 48329202-48329205 and 48339002, and nontarget organism toxicology information in MRID 48329309. The petition for the exemption from the requirement of a tolerance for the new active ingredient tagetes oil is being withdrawn subsequent to the Agency's determination that tagetes oil is exempt from the requirement of a tolerance under 40 CFR 180.950 (refer to the Agency letter to the registrant December 1, 2010).

RECOMMENDATIONS AND CONCLUSIONS

1. The product chemistry submission is UNACCEPTABLE, but upgradeable pending resolution of the deficiencies identified below.

MRID 48329207: UPGRADEABLE MRID 48329208: UPGRADEABLE
MRID 48339001: UPGRADEABLE

Regarding Tagetes Oil:

a. The registrant must verify that the source of tagetes oil will only be obtained by the supplier listed on the CSF. It is unclear to the reviewer from the information submitted in MRID 48329207 as to whether the registrant intends on using different suppliers. The requirement for verification is in reference to the deficiency identified in the memorandum from A.L. Gonzales to C. Walsh dated 8/25/10 (item 1b. in the product chemistry section):

> *"In MRID 47868201 the registrant states that tagetes oil may be supplied by other suppliers/sources than the supplier listed on the CSF. The registrant may only use the supplier/source of an active ingredient that is listed on the CSF and for which data and/or information have been submitted."*

b. The rationale submitted to satisfy the stability data requirement is inadequate for exposure to metals and metal ions. Contact with metals is anticipated and there are no stability data available to the reviewer; subjective statements are not adequate to fulfill the data requirement. These data must be submitted.

c. The UV/Visible absorption data requirement must be satisfied. The registrant has requested to submit this study as a condition of registration; the reviewer recommends that the study be submitted prior to registration as the data are informative for the nontarget organism risk assessment.

d. The rationale provided to satisfy the partition coefficient data requirement is inadequate; statements regarding natural degradation and volatilization are insufficient to satisfy the data requirement. These data must be submitted.

e. All other product chemistry data requirements for tagetes oil have been satisfied at this time.

Regarding Bug Oil Ornamental:

a. The registrant must verify that the sources of canola oil, thyme oil and wintergreen oil will only be obtained by the supplier listed on the CSF. It is unclear to the reviewer from the information submitted in MRID 48329207 as to whether the registrant intends on using different suppliers. The requirement for verification is in reference to the deficiency identified in the memorandum from A.L. Gonzales to C. Walsh dated 8/25/10 (item 1g. in the product chemistry section):

> *"In MRID 47868201 the registrant states that the active ingredients may be supplied by other suppliers/sources than those listed on the CSF. The registrant may only use the supplier/source of*

an active ingredient that is listed on the CSF and for which data and/or information have been submitted."

b. For canola oil, the following physical/chemical property data requirements were not adequately addressed: Stability (OPPTS 830.6313), UV/Visible Light Absorption (OPPTS 830.7050), and Partition Coefficient (OPPTS 830.7550). Subjective information and statements regarding natural degradation are inadequate to satisfy these data requirements. These data are required and must be submitted.

c. For thyme oil, the following physical/chemical property data requirements were not adequately addressed: Stability (OPPTS 830.6313), UV/Visible Light Absorption (OPPTS 830.7050), Boiling Point/Boiling Range (OPPTS 830.7220), Vapor Pressure (OPPTS 830.7950) and Partition Coefficient (OPPTS 830.7550). Although thyme oil is a minimum risk active ingredient under 40 CFR 152.25(f) and products meeting the requirements of this exemption are exempt from certain requirements of FIFRA, the proposed EP does not fall under this exemption; therefore, the data requirements under FIFRA are applicable.

d. The registrant must provide explanations regarding the results of the storage stability and corrosion characteristics study for the EP:

i. The 22.7% loss of wintergreen oil observed at one year, which is substantially outside the lower certified limit for this ingredient.
ii. The lack of storage stability testing for canola oil.
iii. The description of the container: "sides deformed (paneled) and did not regain original shape when bottle opened" after one year of storage.

e. All other product chemistry data requirements have been satisfied at this time.

2. The toxicology submission is ACCEPTABLE pending resolution of the deficiencies listed below.

MRID 48329202: ACCEPTABLE
MRID 48329203: ACCEPTABLE
MRID 48329204: ACCEPTABLE
MRID 48329205: ACCEPTABLE
MRID 48339002: UPGRADEABLE

Regarding Tagetes Oil:

a. The registrant must provide more information regarding the estimated dietary exposure calculations on page 10 of 47 in MRID 48339002. The results of the calculations were provided but the details of the calculations were not. A sample calculation was provided for tagetes oil application to strawberries but did not address the dietary exposure calculation.

b. The registrant must submit the reference, "(FEMA, 1994)" that was cited for the data table provided on page 8 of 47 in MRID 48339002. This reference was unavailable to the reviewer.

c. Adequate data and information were submitted to support the following Tier 1 data requirements: acute inhalation toxicity and mutagenicity: bacterial reverse mutation test.

Regarding Bug Oil Ornamental:

a. Adequate data were submitted to satisfy the acute inhalation toxicity data requirement. All mammalian toxicology data requirements have been fulfilled at this time.

3. The nontarget organism toxicology submission is ACCEPTABLE, pending resolution of the deficiency listed below.
MRID 48329209: ACCEPTABLE

Regarding Tagetes Oil:

a. The information submitted to support the nontarget organism toxicity data requirements for tagetes oil is adequate. However, the risk assessment for nontarget organisms cannot be completed until the product chemistry deficiencies have been sufficiently addressed.

Note to RAL:

1. On the label, in the Personal Protective Equipment (PPE) section, the requirement to wear gloves must be added for handling the diluted product as well as the concentrated product.

STUDY SUMMARIES FOR BUG OIL ORNAMENTAL

Product Chemistry (MRIDs 48329207, 48329208, 48339001)

With the exception of the deficiencies discussed in the **Recommendations and Conclusions** section above, all product chemistry data requirements have been adequately satisfied. Refer to the Confidential Appendix (CA) below for additional information. Data Evaluation Records (DERs) were not created for the submitted MRIDs. For canola oil, the following physical/chemical property data requirements were not adequately addressed: Stability (OPPTS 830.6313), UV/Visible Light Absorption (OPPTS 830.7050), and Partition Coefficient (OPPTS 830.7550). Subjective information and statements regarding natural degradation were provided but are inadequate to satisfy these data requirements. The pH data requirement is not required for canola oil, as it is insoluble in water. The vapor pressure was reported to be < 1 mm Hg at 25°C. For thyme oil, the following physical/chemical property data requirements were not adequately addressed: Stability (OPPTS 830.6313), UV/Visible Light Absorption (OPPTS 830.7050), Boiling Point/Boiling Range (OPPTS 830.7220), Vapor Pressure (OPPTS 830.7950) and Partition Coefficient (OPPTS 830.7550). To satisfy these data requirements, the registrant cited the registration review document for the flower and vegetable oils, under which thyme oil is considered. The registration review for these ingredients is pending and a final decision has not been issued. Refer to http://www.epa.gov/oppsrrd1/registration_review/vegetable-and-flower-oils/index.html for more information. In this document, it is stated the physical and chemical properties data requirements were not required. Although thyme oil is a minimum risk active ingredient under 40 CFR 152.25(f) and products meeting the requirements of this exemption are exempt from certain requirements of FIFRA, the proposed EP does not fall under this exemption; therefore, the data requirements under FIFRA are applicable. For wintergreen oil, adequate information was submitted to

fulfill the outstanding data requirements. A storage stability and corrosion characteristics study was submitted in MRID 48339001 on the EP. The study is adequate with the following exceptions: 1) there was a 22.7% loss of wintergreen oil observed at one year, which is substantially outside the lower certified limit for this ingredient; 2) storage stability testing was not conducted for canola oil; 3) in the corrosion characteristics portion there was a description of the container: "sides deformed (paneled) and did not regain original shape when bottle opened", which must be explained. There was some loss observed in the amounts of thyme oil and tagetes oil but the amounts remained within the certified limits. Beside the container changes noted above, there were no other changes observed in the corrosion characteristics study.

Mammalian Toxicology (MRIDs 48329202, 48329204)

All mammalian toxicology data requirements have been satisfied for Bug Oil Ornamental. A summary of the data requested by the Agency which was submitted for Bug Oil Ornamental is provided in Table 1 below. A guideline acute inhalation toxicity study was submitted to satisfy the acute inhalation toxicity data requirement. Although not required, a mutagenicity study (Ames test) was conducted on the EP and submitted to the Agency. DERs were not created for these MRIDs.

Table 1. Mammalian Toxicology Data Requirements for *Bug Oil Ornamental* (40 CFR § 158.2050)

Study/OPPTS Guideline No.	Results	Toxicity Category/Description	MRID
Acute inhalation toxicity (rat) (870.1300)	LC_{50} > 5.22 mg/L	IV	48329202
Bacterial reverse mutation test (Ames) (870.5100)	Not mutagenic with or without metabolic activation in *Salmonella typhimurium* strains TA 98, TA 1537, TA 100, TA 1535 and *Escherichia coli* strain Wp2uvrA	N/A	48329204

ADDITIONAL INFORMATION AND STUDY SUMMARIES FOR THE RISK ASSESSMENT FOR TAGETES OIL

Refer to the memorandum from A.L. Gonzales to C. Walsh dated 8/25/10 for the initial risk assessment and summaries of data submitted for tagetes oil.

I. Active Ingredient Characterization

A. Product Chemistry (MRIDs 48329207, 48329208, 48339001)

With the exception of the deficiencies discussed in the **Recommendations and Conclusions** section above, all product chemistry data requirements have been adequately satisfied. The data requested by the Agency which were submitted to support the product chemistry data requirements are summarized in Table 2 below. Data Evaluation Records were not created for the submitted MRIDs. The registrant provided inadequate rationale to satisfy the stability to metals and metal ions data requirement. Contact with metals is anticipated and there were no stability data available to the reviewer; subjective

statements are not adequate to fulfill the data requirement. Stability data to elevated temperatures were available from the storage stability study in MRID 48339001 and indicated that tagetes oil is stable to elevated temperatures. The registrant requested to submit the UV/Visible absorption study as a condition of registration; the reviewer recommends that the study be submitted prior to registration as the data are informative for the nontarget organism risk assessment. The rationale provided to satisfy the partition coefficient data requirement was inadequate; statements regarding natural degradation and volatilization are insufficient to satisfy the data requirement. The vapor pressure data requirement was adequately addressed.

TABLE 2. Physical and Chemical Properties of Tagetes Oil (40 CFR § 158.2030)

OPPTS Guideline No.	Property	Description of Result	MRID
830.6313	Stability to Normal and Elevated Temperatures, Metals and Metal Ions	Stable to normal and elevated temperatures. **Rationale provided for stability to metals is inadequate.**	48329208 48339001
830.7050	UV/Visible light absorption	Request to submit study as a condition of registration.	48329208
830.7550 830.7560 830.7570	Partition Coefficient (n-Octanol/Water)	**Rationale provided for stability to metals is inadequate.**	48329208
830.7950	Vapor Pressure	Approximately 59% volatilization (measured via weight loss) in 48 hours in laboratory study.	48329208

II. Human Health Assessment

A. Toxicology (MRIDs 48329203, 48329205, 48339002)

A guideline acute inhalation toxicity study was submitted to satisfy the acute inhalation toxicity data requirement and a guideline bacterial reverse mutation test was submitted to satisfy the mutagenicity data requirement. Rationale was provided to satisfy the remaining Tier 1 data requirements. With the exception of the deficiencies discussed in the **Recommendations and Conclusions** section above, adequate mammalian toxicology data and information have been submitted to satisfy all of the Tier 1 toxicology data requirements at this time. The data and information presented in Table 3 below are a summary of the toxicity data and information submitted to support the new active ingredient, Tagetes Oil. DERs were not created for these MRIDs.

Table 3. Mammalian Toxicology Data Requirements for Tagetes Oil (40 CFR § 158.2050)			
Study/OPPTS Guideline No.	**Results**	**Toxicity Category/Description**	**MRID**
Acute inhalation toxicity (870.1300)	LC_{50} > 5.20 mg/L	IV	48329203
90-Day oral toxicity (870.3100)	Rationale was provided in lieu of a 90-day oral study. Tagetes oil is exempt from the requirement of a tolerance as a minimal risk active ingredient under 40 CFR 158.950(c). Significant exposure is not expected based on low application rates and rapid degradation in the environment. Once the additional data requested by the Agency (refer to the **Recommendations and Conclusions** section above) are received and reviewed, this assessment will be completed.		48339002
90-Day inhalation toxicity (870.3465)	Rationale was provided in lieu of a 90-day inhalation study. Significant exposure to humans to tagetes oil as a gas, vapor or aerosol is not anticipated. Additionally, significant exposure is not expected based on low application rates and rapid degradation in the environment. Once the additional data requested by the Agency (refer to the **Recommendations and Conclusions** section above) are received and reviewed, this assessment will be completed.		48339002
Mutagenicity (Ames) (870.5100, 5300 and 5375)	Not mutagenic with or without metabolic activation in *Salmonella typhimurium* strains TA 98, TA 1537, TA 100, TA 1535 and *Escherichia coli* strain Wp2uvrA. Rationale was provided in lieu of an *in vitro* mammalian cell assay. Significant exposure to humans is not anticipated based on low application rates, appropriate PPE requirements on the label, and rapid degradation in the environment. Once the additional data requested by the Agency (refer to the **Recommendations and Conclusions** section above) are received and reviewed, this assessment will be completed.		48329205
Developmental toxicity (870.3700)	Rationale was provided in lieu of a developmental study. Significant exposure to female humans is not anticipated based on low application rates, appropriate PPE requirements on the label, and rapid degradation in the environment. Once the additional data requested by the Agency (refer to the **Recommendations and Conclusions** section above) are received and reviewed, this assessment will be completed.		48339002

1. Acute Toxicity

Tagetes is of low acute inhalation toxicity; there were no mortalities at the 5.20 mg/L dose.

2. Subchronic Toxicity

90-Day Oral

Rationale was provided in lieu of a 90-day oral study. Tagetes oil is exempt from the requirement of a tolerance as a minimal risk active ingredient under 40 CFR 158.950(c). Significant dietary exposure to humans is not anticipated based on low application rates and rapid biodegradation in the environment. Based on data provided in MRID 48329208, approximately 59% of tagetes oil volatilized (measured via weight loss) in 48 hours in laboratory study. Once the additional data requested by the Agency (refer to the **Recommendations and Conclusions** section above) are received and reviewed, the 90-day oral toxicity and dietary assessment will be completed.

90-Day Inhalation

Rationale was provided in lieu of a 90-day inhalation study. Significant exposure to humans to tagetes oil as a gas, vapor or aerosol is not anticipated. Additionally, significant exposure is not expected based on low application rates and rapid degradation in the environment. Once the additional data requested by the Agency (refer to the **Recommendations and Conclusions** section above) are received and reviewed, this assessment will be completed.

3. Developmental Toxicity and Mutagenicity

Rationale was provided in lieu of a developmental study. Significant exposure to female humans is not anticipated based on low application rates, appropriate PPE requirements on the label, and rapid degradation in the environment. Once the additional data requested by the Agency (refer to the **Recommendations and Conclusions** section above) are received and reviewed, this assessment will be completed.

In an Ames assay, concentrations of up to 5,000 µg/plate of tagetes oil were not mutagenic with or without metabolic activation (S9) in *Salmonella typhimurium* strains TA 98, TA 1537, TA 100, TA 1535 and *Escherichia coli* strain Wp2uvrA. Rationale was provided in lieu of an *in vitro* mammalian cell assay. Significant exposure to humans is not anticipated based on low application rates, appropriate PPE requirements on the label, and rapid degradation in the environment. Once the additional data requested by the Agency (refer to the **Recommendations and Conclusions** section above) are received and reviewed, this assessment will be completed.

B. Dose Response Assessment

At this time, no endpoints have been identified; therefore, a dose response assessment is not required.

C. Food Quality Protection Act (FQPA) Considerations

1. Dietary Exposure and Risk Characterization

A dietary exposure and risk assessment will be conducted once all product chemistry and mammalian toxicology data requirements have been satisfied.

2. Acute and Chronic Dietary Risks for Sensitive Subpopulations Particularly Infants and Children

An acute and chronic dietary risk assessment for sensitive subpopulations will be conducted once all product chemistry and mammalian toxicology data requirements have been satisfied.

D. Drinking Water Exposure and Risk Characterization

Once all physical and chemical properties data requirements are satisfied, the drinking water exposure and risk assessment will be conducted.

E. Occupational, Residential, School and Day Care Exposure and Risk Characterization

1. Occupational Exposure and Risk Characterization

An occupational exposure assessment will be conducted once all product chemistry and mammalian toxicology data requirements have been satisfied.

2. Residential, School and Day Care Exposure and Risk Characterization

Exposure to tagetes oil will be minimal in residential, school, and day care areas, as the product containing this active ingredient is intended for use on horticultural and agricultural crops.

F. Aggregate Exposure from Multiple Routes Including Dermal, Oral, and Inhalation

The aggregate exposure assessment will be conducted once all product chemistry and mammalian toxicology data requirements have been satisfied.

G. Cumulative Effects

Cumulative effects will be assessed once all product chemistry and mammalian toxicology data requirements have been satisfied.

H. Risk Characterization

The risk assessment will be conducted once all product chemistry and mammalian toxicology data requirements have been satisfied.

III. Environmental Assessment

A. Nontarget Organism Toxicology (MRID 48329209)

Toxicity studies have not been submitted for tagetes oil. Rationale and data on the proposed EP have been submitted to fulfill these data requirements. According to the registrant, the active ingredients act synergistically; thus the combination of these chemicals is more potent as an insecticide than each ingredient alone. Therefore, the toxicological profile of the EP is germane to the risk assessment rather than the toxicological profile of tagetes oil alone. For registration of the proposed EP, the Agency will bridge the nontarget organism toxicology data from the EP to the TGAI, tagetes oil.

B. Environmental Fate and Groundwater Data

Environmental fate and groundwater data are not required at this time because the results of the nontarget organism toxicity assessment (Tier I data requirements) did not trigger these Tier II data requirements.

C. Ecological Exposure and Risk Characterization

A ecological risk assessment will be conducted once all product chemistry data requirements have been satisfied.

CONFIDENTIAL APPENDIX

STUDY SUMMARIES FOR BUG OIL ORNAMENTAL

Product Chemistry (MRIDs 48329207, 48329208, 48339001)

The registrant must verify that the sources of canola oil, thyme oil and wintergreen oil will only be obtained by the supplier listed on the CSF. It is unclear to the reviewer from the information submitted in MRID 48329207 as to whether the registrant intends on using different suppliers. Information on purchasing requirements for the suppliers of the oils was provided, but there was no statement or correction to the original statement in MRID 47868201 that multiple suppliers may be used. The requirement for verification is in reference to the deficiency identified in the memorandum from A.L. Gonzales to C. Walsh dated 8/25/10 (item 1g. in the product chemistry section):

"In MRID 47868201 the registrant states that the active ingredients may be supplied by other suppliers/sources than those listed on the CSF. The registrant may only use the supplier/source of an active ingredient that is listed on the CSF and for which data and/or information have been submitted."

The CSF was adequately revised according to the Agency's requirements and recommendations. [redacted]

ADDITONAL INFORMATION AND STUDY SUMMARIES FOR THE RISK ASSESSMENT FOR TAGETES OIL

A. Product Chemistry (MRIDs 48329207, 48329208, 48339001)

[redacted] The registrant must verify that the source of tagetes oil will only be obtained by the supplier listed on the CSF. It is unclear to the reviewer from the information submitted in MRID 48329207 as to whether the registrant intends on using different suppliers. Information on purchasing requirements for the supplier of tagetes oil was provided, but there was no statement or correction to the original statement in MRID 47868201 that multiple suppliers may be used. The requirement for verification is in reference to the deficiency identified in the memorandum from A.L. Gonzales to C. Walsh dated 8/25/10 (item 1b in the product chemistry section):

"In MRID 47868201 the registrant states that tagetes oil may be supplied by other suppliers/sources than the supplier listed on the CSF. The registrant may only use the supplier/source of an active ingredient that is listed on the CSF and for which data and/or information have been submitted."

cc: Angela L. Gonzales, Colin Walsh, BPPD Science Review File, IHAD/ARS
A. L. Gonzales, FT, PY-S: 6/23/11